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(54) Methods for accurate sequence data and modified base position determination

(57) Disclosed herein are methods of determining the sequence and/or positions of modified bases in a nucleic acid sample present in a circular molecule with a nucleic acid insert of known sequence comprising obtaining sequence data of at least two insert-sample units. In some embodiments, the methods comprise obtaining sequence data using circular pair-locked molecules. In some embodiments, the methods comprise calculating scores of sequences of the nucleic acid inserts by comparing the sequences to the known sequence of the nucleic acid insert, and accepting or rejecting repeats of the sequence of the nucleic acid sample according to the scores of one or both of the sequences of the inserts immediately upstream or downstream of the repeats of the sequence of the nucleic acid sample.

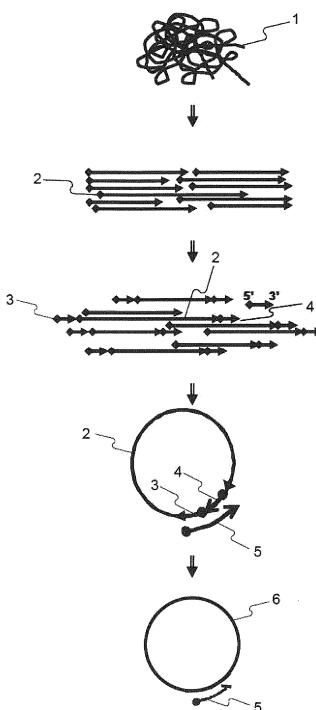


Fig. 1



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Application Number

EP 14 15 0163

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X, P	WO 2009/120372 A2 (PACIFIC BIOSCIENCES CALIFORNIA [US]; TRAVERS KEVIN [US]; OTTO GEOFF [U] 1 October 2009 (2009-10-01) * claims 12-22 * * paragraphs [0078], [0093], [0098] * * figure 2B * -----	17,21	INV. C12Q1/68 G06F19/22
Y	US 2007/020640 A1 (MCCLOSKEY MEGAN L [US] ET AL) 25 January 2007 (2007-01-25) * figures 1,3,4 * * paragraphs [0002], [0008], [0010], [0015], [0016], [0018] - [0020], [0022], [0031], [0034], [0036] * * example 6 * -----	1-16,19, 20	
Y	US 6 087 099 A (GUPTA JAMILA [US] ET AL) 11 July 2000 (2000-07-11) * claims 1-3 * * column 2, line 14 - line 38 * * figure 2 * -----	1-16,19, 20	
Y	US 2001/039039 A1 (WEISSMAN SHERMAN [US] ET AL) 8 November 2001 (2001-11-08) * figure 2 * * paragraphs [0017], [0027], [0033], [0034], [0037] * -----	1-16,19, 20	TECHNICAL FIELDS SEARCHED (IPC) C12Q G06F
		-/-	
1	The present search report has been drawn up for all claims		
	Place of search	Date of completion of the search	Examiner
	Munich	11 July 2014	Schmitt-Humbert, C
	CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background C : non-written disclosure P : intermediate document		
	T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document		



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Application Number

EP 14 15 0163

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45

50

55

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	LAIRD CHARLES D ET AL: "Hairpin-bisulfite PCR: Assessing epigenetic methylation patterns on complementary strands of individual DNA molecules", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, NATIONAL ACADEMY OF SCIENCES, US, vol. 101, no. 1, 6 January 2004 (2004-01-06), pages 204-209, XP002535768, ISSN: 0027-8424, DOI: 10.1073/PNAS.2536758100 * abstract * * figures 1,2 * * page 204, column 2, last paragraph - page 206, column 1, paragraph 2 * -----	1-16,19,20	
Y	B. E. MINER: "Molecular barcodes detect redundancy and contamination in hairpin-bisulfite PCR", NUCLEIC ACIDS RESEARCH, vol. 32, no. 17, 23 September 2004 (2004-09-23), pages e135-e135, XP55099281, DOI: 10.1093/nar/gnh132 * abstract * * page 1, column 2, paragraph 2 - page 2, column 1, paragraph 2 * * figures 1,2 * -----	1-16,19,20	TECHNICAL FIELDS SEARCHED (IPC)
Y	T. MATSUMURA ET AL: "Photochemical transition of 5-methylcytosine to thymine by DNA photoligation", NUCLEIC ACIDS SYMPOSIUM SERIES, vol. 51, no. 1, 1 November 2007 (2007-11-01), pages 233-234, XP055128235, ISSN: 0261-3166, DOI: 10.1093/nass/nrm117 * abstract * -----	6	
The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
Munich		11 July 2014	Schmitt-Humbert, C
CATEGORY OF CITED DOCUMENTS			
X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document			
T: theory or principle underlying the invention E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons &: member of the same patent family, corresponding document			

ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.

EP 14 15 0163

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This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

11-07-2014

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	Patent document cited in search report	Publication date		Patent family member(s)	Publication date
15	WO 2009120372 A2	01-10-2009	AU	2009229157 A1	01-10-2009
			CA	2719747 A1	01-10-2009
			CN	102084001 A	01-06-2011
			EP	2274449 A2	19-01-2011
20			JP	2011515102 A	19-05-2011
			US	2009298075 A1	03-12-2009
			US	2011281768 A1	17-11-2011
			US	2012289408 A1	15-11-2012
			US	2013309678 A1	21-11-2013
			WO	2009120372 A2	01-10-2009
25	US 2007020640 A1	25-01-2007		NONE	
	US 6087099 A	11-07-2000	US	6087099 A	11-07-2000
			US	6251610 B1	26-06-2001
			US	6258544 B1	10-07-2001
30	US 2001039039 A1	08-11-2001	US	6235502 B1	22-05-2001
			US	2001039039 A1	08-11-2001
			US	2002076704 A1	20-06-2002
35					
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55					

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82